REMARKS

Prior to this Response, claims 7-38 were pending in this application. Claims 1-6 were previously canceled, and in this Response claims 13-14, 26-28, and 38 are canceled, all without prejudice or disclaimer of the subject matter therein, leaving claims 7-12, 15-25 and 29-37 currently pending. Claims 22-25 were previously withdrawn from consideration as being directed to a non-elected invention, and in the Office Action dated July 22, 2008, claims 34-37 were similarly withdrawn from consideration as being directed to a non-elected invention; reconsideration of the withdrawal of claims is discussed in detail below.

In this Response, claims 7, 12, 15-18, 32, and 36 have been amended. The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Basis for the claim amendments is found in paragraphs 0040 and 0092 of the application as published; in claims 1-25 as originally filed; and elsewhere throughout the specification and claims. Accordingly, entry of the amendments is respectfully requested.

Allowable Subject Matter. Applicants acknowledge and thank the Examiner for the indication that claims 12 and 15-17 and new claims 30-33 would be allowable if rewritten in independent form. In light of the amnedments and arguments presented in this Response, Applicants respectfully submit that additional claims are allowable and have not, at this time, rewritten any claim in independent form.

Rejections withdrawn. Applicants acknowledge and thank the Examiner for withdrawing the following rejections under 35 U.S.C. 102, Applicant's arguments have been fully considered and found persuasive as to overcoming the following cited references: Mishin et al., Zhang et al., Sumiyoshi et al., and Chang et al. Applicants further acknowledge and thank the Examiner for withdrawing the following rejections

under 35 U.S.C. 103, Applicant's arguments have been fully considered and found persuasive as to overcoming the following cited references: (1) Zhang et al. and Sumiyoshi et al. in view of Chang et al., and (2) Zhang et al. and Sumiyoshi et al. in view of Schumacher et al.

1. Withdrawal of claims 22-25 and 34-37

The Office Action indicates that new claims 34-37 are withdrawn because they are directed to a non-elected invention. Claims 22-25 were previously withdrawn for the same reason.

Applicants respectfully traverse the withdrawal of these claims, on the ground that the withdrawn claims are so closely related to claims under examination that the differences are inconsequential. In particular, Applicants respectfully submit that the claims should not be restricted to the species SEQ. ID. No. 45, because the nucleotide sequences of SEQ. ID. Nos. 45 and 48 differ ***only*** in that SEQ. ID. No. 48 additionally includes a prokaryotic promoter for *in vitro* transcription, and are otherwise identical. Thus, claims directed to SEQ. ID. No. 48 would properly be dependent on claims directed to SEQ. ID. No. 45. Thus, it is not a burden to search and examine both the nucleotide sequences in claims 12, 15-17, 31 and 32.

Applicants respectfully request that the Examiner reinstate, examine, and allow claims 22-25 and 34-37.

2. Objections to claims 12, 15-17, 31-32, and 38

The Office Action maintains the objection to claims 12 and 15 because the claims contain multiple sequence identifiers, which are drawn to nonelected inventions. Claims

16, 17, 31 and 32 are newly objected to because of the following informalities: The claims contain vectors represented by SEQ 10 NO: 45 however the sequence identifiers are not listed in the claims. Appropriate correction is required. Claim 38 is objected to because of the following informalities: The claim is dependent on a withdrawn claim. Appropriate correction is required.

With regard to claims 12 and 15, Applicants have amended to delete non-elected species. Claim 38 has been canceled.

Applicants respectfully traverse the remaining objections to the claims: as discussed above, Applicants respectfully submit that it should not be required to delete SEQ. ID. No: 48 from the claims; the only difference between SEQ. ID. Nos: 45 and 48 is the addition of a prokaryotic promoter for in vitro transcription, and a search of SEQ. ID. No: 45 is effectively a search of SEQ. ID. No: 48. Thus, it is respectfully submitted that it is not a burden to search and examine both of the nucleotide sequences in claims 12, 15-17, 31 and 32. Further, Applicants respectfully point out that the Examiner has already substantially examined the cDNA clone of JEV, having the nucleotide sequence of SEQ. ID. No: 48, and has only objected to claim 16 as not specifying a particular SEQ. ID. No., while noting that claim 16 is free of the prior art.

Accordingly, the Examiner is respectfully requested to withdraw these objections.

3. Rejection of claims 16 and 17 under 35 USC §112, first paragraph (enablement)

The Office Action rejects claims 16 and 17 under 35 U.S.C. §112, first paragraph, as lacking enablement for the following reasons:

> The specification has a reference to the deposit of vectors however the address of the depository is not listed in the body of the specification. The

> deposit must be referred to in the body of the specification and be identified by deposit (accession) number, name and address of the depository, and the complete taxonomic description. Appropriate correction is required.

Applicants thank the Examiner for her comments. 37 CFR 1.809(d) requires the following:

> For each deposit made pursuant to these regulations, the specification shall contain:
> (1) The accession number for the deposit;
> (2) The date of the deposit;
> (3) A description of the deposited biological material sufficient to specifically identify it and to permit examination; and
> (4) The name and address of the depository.

Applicants have amended the Specification as required by 37 CFR 1.809(d), to include the address of the depository. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

4. Rejection of claims 26 and 27 under 35 USC §112, second paragraph

The Office Action rejects claims 26 and 27 under 35 U.S.C. §112, second paragraph, as being indefinite, for the following reasons:

> The claims the phrase "elements originated from" which does not distinctly define the claimed invention because the term "elements" which is not defined in the specification is indefinite.

Applicants have canceled claims 26 and 27, obviating this ground of rejection. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

5. Rejection of claim 28 under 35 USC §112, second paragraph

The Office Action rejects claim 28 under 35 U.S.C. §112, second paragraph, as being indefinite, for the following reasons:

> Claim 28 is drawn to a therapeutic agent comprising the JEV cDNA of claim 7 as effective ingredients. Claim 7 is drawn to a cDNA clone, which contains more than just the cDNA. Therefore claim 28 fails to particularly point out and distinctly claim the subject matter of the claimed invention.

Applicants have canceled claim 28, obviating this ground of rejection. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

6. Rejection of claims 7-11, 13-14, 18-21, and 26-29 under 35 USC §112, first paragraph (enablement)

The Office Action rejects claims 7-11, 13-14, 18-21, and 26-29 under 35 U.S.C. §112, first paragraph, as lacking enablement, for the following reasons:

> [T]he specification, while being enabling for a vector represented by SEQ 10 NO: 45, pBACsP6/JVFLx/Xbal, comprising a full length infectious and genetically stable cDNA clone of JEV, does not reasonably provide enablement for a full length infectious and genetically stable cDNA clone of JEV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.
>
> The nature of the invention: The claimed invention is drawn to a full length infectious and genetically stable cDNA clone of JEV encompassed in a BAC vector, pBACSP6/JVFLx/Xbal, represented by SEQ 10 NO: 45 and having a SP6 or T7 promoter.
>
> The state of the prior art: The art teaches that a full-length stable clone of JEV was not infectious. The art teaches that transcripts of the full-length PCR amplicon from the cDNA clone of JEV produced infectious virus. The art further teaches that transfection of cultured cells with the full-length cDNA amplicons or clone failed to produce infectious viruses as described by Zhang et al. (Journal of Virological Methods, August 2001, Vol. 96, No.2, pages 171-182). Zhang et al. also teaches the transcript from the clone was non-infectious, however, the transcript from the amplicon of the clone was infectious (page 180, top of 2nd col.).
>
> The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability in the art regarding the structural and functional differences in the JEV clone, detailed teachings are required in the disclosure to enable the full scope of the claims. These teachings are absent. Applicant's disclosure is limited to the cDNA clone of JEV in BAC vectors. The only working examples are for

clones encompassed in BAC vectors and having a SP6 or T7 promoter. Examples are provided for the BAC vectors; however, no examples are provided for a full length infectious cDNA clone of JEV in the absence of a BAC vector.

The breadth of the claims and the quantity of experimentation needed: Because the invention encompasses full length infectious cDNA clones of JEV and because the specification fails to provide guidance as to how to use the claimed method for full length infectious cDNA clones of JEV other than full length infectious cDNA clones of JEV in BAC vectors, it would require undue experimentation by one of skill in the art to be able to practice the claimed invention commensurate in scope with the claims.

Applicants have amended claim 7 to claim a full length infectious and genetically stable cDNA clone of JEV which is inserted into a BAC plasmid. Thus, Applicants respectfully submit that the specification provides enablement for the amended claim 7 and dependent claims thereof.

Accordingly, the Examiner is respectfully requested to withdraw this rejection.

7. Rejection of claims 18-21, 26-28 and 38 under 35 U.S.C. 102(b)

The Office Action rejects claims 18-21, 26-28 and 38 under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (Journal of Virological Methods, Aug. 2001, Vol. 96, No.2, pages 171-182), for the following reasons:

The claimed invention is drawn to an infectious JEV RNA transcript synthesized from the cDNA clone, which is a full length infectious and genetically stable cDNA of JEV, wherein virus-unrelated nucleotides at its 3' end are removed. The claimed invention is also drawn to a cell transfected with the JEV RNA transcript. The claimed invention is also drawn to a diagnostic reagent and an anti-JEV vaccine containing elements originated from the JEV cDNA clone (described above). The claimed invention is also drawn to a therapeutic agent comprising the JEV cDNA.

Zhang et al. (hereinafter Zhang) teaches a technique to produce genome length cDNA stable clone from Japanese encephalitis virus (Abstract). The cDNA has a T7 promoter at the 5' end and a "run-off' transcript with vector sequences at either end (Abstract). The full-length amplicon was cloned

into a vector under the SP6 promoter (Abstract). The RNA transcript was synthesized from the clone (page 174-175, connecting paragraph). Zhang teaches Japanese encephalitis virus genome lacks a poly-A tail at the 3'-terminus (page 176, 1st column). Zhang teaches RNA transcripts were transfected into BHK-21 cells (page 175, 1st column, 1st paragraph). Zhang teaches Japanese encephalitis virus has short untranslated regions (page 172, 1st column, 1st paragraph). Zhang teaches amplification of the full-length JEV genome by novel long RT-PCR protocol, transcription of infectious RNA directly from the amplicon and construction of a stable full-length JEV cDNA clone (page 173, 1st column, 2nd paragraph). Zhang also teaches the transcript from the clone was non-infectious, however, the transcript from the amplicon of the clone was infectious (page 180, top of 2nd col.).

Applicants have canceled claims 26-28 and 38. As to remaining claims 18-21, Applicants respectfully traverse this rejection. Anticipation under 35 USC §102 requires that a single prior art reference describe each and every element of the claimed invention. *See Verdegaal Bros. v. Union Oil Co. of California,* 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.,* 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond,* 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants respectfully submit that Zhang et al. do not teach each and every element of claims 18-21, as required for anticipation under 35 USC §102. Independent claim 18 refers to claim 7, which, as amended, is directed to "A full length infectious and genetically stable cDNA clone of Japanese encephalitis virus (JEV), wherein a full length cDNA of JEV is cloned into a BAC vector." Claims 19-21 depend, either directly or indirectly, from claim 18.

The claims as amended are allowable because the special technical feature of the present invention is that it is possible to provide a full length and genetically stable cDNA clone by cloning a full length cDNA of JEV into a BAC plasmid.

No prior art teaches or suggests, for purposes of sections 102 and 103, incorporating a full length cDNA of JEV into a BAC plasmid.

Zhang et al. failed to establish a full length and genetically stable infectious cDNA clone of JEV. Zhang et al. made a JEV cDNA clone via cloning a full length cDNA into cosmid vector, but the clone is not infectious. Rather, Zhang et al. performed long PCR using the cDNA clone as a template and then performed in vitro transcription in order to an infectious JEV RNA transcript. Zhang et al. neither teaches nor suggest an infectious full length RNA transcript transcribed directly from full length cDNA clone of JEV. Thus, amended claims 18-21 should be allowed.

Further, although Fernando et al. (Proc. Natl. Acad. Soc. U.S.A., 98(10): 5516-5521, 2000, submitted by Applicants in an earlier IDS filing) teaches that a BAC plasmid is used for cloning a infectious cDNA clone of coronavirus, the only reason for using a BAC plasmid is that the BAC plasmid can be used to clone **large DNA fragments** stably from a variety of complex genomic source into bacteria. Further, Shizuya et al. (Proc. Natl. Acad. Soc. U.S.A., 89: 8794-8797, 1992) cited by Fernando et al. (copy attached) teaches that it is capable of maintaining human genomic DNA fragments of >300 kilobase pairs and that individual clones of human DNA appear to be maintained with a high degree of structural stability in the host, even after 100 generations of serial growth. Thus, a skilled artisan will understand that the utility for BAC plasmids is stably cloning large DNA sequences.

Conversely, the size of the JEV genome is only 11 kb, which is one third of that of the coronavirus cloned by Fernando et al. and more than an order of magnitude smaller than the usual sequences cloned using BAC plasmids. Thus, if the size of genome caused trouble for cloning cDNA of JEV, a skilled artisan would use a

phagemid or a cosmid as the vector. However, the attempt to clone an infectious cDNA of JEV into a cosmid was a complete failure (See Zhang et al., 2001, which is cited by the Examiner in the present Office Action).

Further, Fernando et al. utilizes a highly complex strategy requiring numerous manipulations of DNA, such as removing some Cla I sites and reintroducing them. Further, one skilled in the art cannot simply deduce the instant invention from a combination with Ymshchikov et al. (Virology, 281(2): 272-280, 2001, which was cited in the prosecution procedure of the EPO and is submitted herewith as an IDS document).

For many RNA viruses, the genetic instability of the cloned cDNA during its construction is particularly problematic. The JEV is also a kind of RNA virus. For this reason, despite previously conducted extensive attempts, it has been reported that to acquire a genetically stable full-length infectious JEV cDNA clone was very difficult (see discussion at page 20, line 7 to 20 of the specification as filed originally).

In addition, it is noted that the Examination Division of the EPO has acknowledged novelty and inventive step of the present invention (See the Examination Report and claim set being examined by the EPO Examination Division, attached to the accompanying IDS).

Therefore, it is submitted that Zhang et al. fails to teach each and every element of the presently pending claims 18-21 as required for anticipation under 35 USC §102(b). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

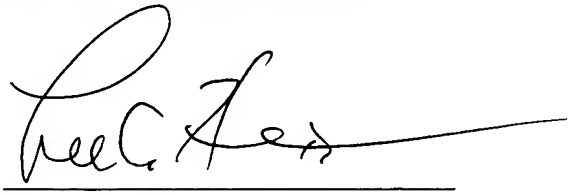
Based upon the above remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is

therefore respectfully requested to reconsider and withdraw the rejections of remaining claims 7-12, 15-25 and 29-37 and allow all pending claims presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this application is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

Respectfully submitted,

THE NATH LAW GROUP

Dated: January 21, 2009

By: 

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